

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1-28 (Cancelled)

29. (Currently Amended) A composition for treating or preventing arthritis or other degenerative disease, said composition comprising ~~an anti-arthritic or anti-inflammatory~~ one or more polypeptide fragment, ~~wherein the polypeptide~~ having at least 65% amino acid identity to SEQ ID NO:14, and wherein said fragment induces tolerance to cartilage.

30. (Previously Presented) The composition of claim 29, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

31. (Previously Presented) The composition of claim 29, wherein the polypeptide has an amino acid length of less than 250 amino acids.

32. (Currently Amended) The composition of claim 29, wherein the ~~NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having~~ has identity to ~~SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18~~ that is:

- a) at least ~~80~~ 70%;
- b) at least 90%; or
- c) 100%.

33. (Currently Amended) The composition of claim 29, wherein the composition comprises one or more polypeptide ~~comprises~~ fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20]
- (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21]
- (c) KLGNNVDFRI [SEQ ID NO: 4]
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22]
- (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23]

- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24]
- (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25]
- (h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26]
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) ~~residues Ile21–Gly182 of SEQ ID NO: 1;~~
- (ii) ~~residues Lys60–Arg181 of SEQ ID NO: 1;~~
- (iii) ~~residues Arg72–Arg181 of SEQ ID NO: 1;~~
- (iv) ~~residues Lys98–Gly182 of SEQ ID NO: 1;~~
- (v) ~~residues Lys123–Gly182 of SEQ ID NO: 1;~~
- (vi) ~~residues Ile24–Val208 of SEQ ID NO: 14;~~
- (vi) ~~residues Asp29–Val208 of SEQ ID NO: 14;~~
- (vii) ~~residues Asp29–Met215 of SEQ ID NO: 14;~~
- (viii) ~~residues Asp29–Pro209 of SEQ ID NO: 14;~~
- (ix) ~~residues Asp29–Arg245 of SEQ ID NO: 14;~~
- (x) ~~residues Asp29–Met96 of SEQ ID NO: 14, or~~
- (xi) ~~residues Trp108–Val208 of SEQ ID NO: 14.~~

34. (Currently Amended) The composition of claim 29, wherein the composition comprises one or more polypeptide comprises fragment selected from at least one of SEQ ID NOs: 2–11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28]
- (b) KIMIGVERTS [SEQ ID NO: 3,10]
- (c) RIESLPIKPRG [SEQ ID NO: 5]
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29]
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30]
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31]
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]
- (h) RSSATLFDVCNRI [SEQ ID NO: 11]

35. (Currently Amended) A method of inducing tolerance to at least one antigenic component of cartilage in an individual, the method comprising administering to the individual the composition of claim 29, wherein said administering induces said tolerance.

36. (Previously Presented) The method of claim 35, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

37. (Previously Presented) The method of claim 35, wherein the polypeptide has an amino acid length of less than 250 amino acids.

38. (Currently Amended) The method of claim 35, wherein the ~~NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having~~ has identity to SEQ ID NO: 1, SEQ ID NO: 14, ~~SEQ ID NO: 16, or SEQ ID NO: 18~~ that is:

- a) at least ~~80~~ 70%;
- b) at least 90%; or
- c) 100%.

39. (Currently Amended) The method of claim 35, wherein the composition comprises one or more polypeptide ~~comprises~~ fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20]
- (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21]
- (c) KLGNVDFRI [SEQ ID NO: 4]
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22]
- (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23]
- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24]
- (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25]
- (h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26]
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) — ~~residues Ile21—Gly182 of SEQ ID NO: 1;~~
- (ii) — ~~residues Lys60—Arg181 of SEQ ID NO: 1;~~
- (iii) — ~~residues Arg72—Arg181 of SEQ ID NO: 1;~~
- (iv) — ~~residues Lys98—Gly182 of SEQ ID NO: 1;~~

- (v) ~~residues Lys123-Gly182 of SEQ ID NO: 1;~~
- (vi) ~~residues Ile24-Val208 of SEQ ID NO: 14;~~
- (vii) ~~residues Asp29-Val208 of SEQ ID NO: 14;~~
- (viii) ~~residues Asp29-Met215 of SEQ ID NO: 14;~~
- (ix) ~~residues Asp29-Pro209 of SEQ ID NO: 14;~~
- (x) ~~residues Asp29-Arg245 of SEQ ID NO: 14;~~
- (xi) ~~residues Asp29-Met96 of SEQ ID NO: 14; or~~
- (xii) ~~residues Trp108-Val208 of SEQ ID NO: 14.~~

40. (Currently Amended) The method of claim 35, wherein the composition comprises one or more polypeptide comprises fragment selected from at least one of SEQ ID NOs: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28]
- (b) KIMIGVERTS [SEQ ID NO: 3,10]
- (c) RIESLPIKPRG [SEQ ID NO: 5]
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29]
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30]
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31]
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]
- (h) RSSATLTFVDCNRI [SEQ ID NO: 11].

41. (Previously Presented) The method of claim 35, wherein the individual is a naive individual.

42. (Currently Amended) The method of claim 35, A method for treating or preventing wherein said administering treats or prevents a degenerative condition or disease in an individual comprising administering to the individual the composition of claim 29.

43. (Previously Presented) The method of claim 42, wherein the degenerative condition or disease is arthritis or a musculoskeletal degenerative condition.

44. (Previously Presented) The method of claim 43, wherein the degenerative condition or disease is rheumatoid arthritis, osteoarthritis, disc degeneration, or osteoporosis.

45. (Previously Presented) The method of claim 42, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

46. (Previously Presented) The method of claim 42, wherein the polypeptide has an amino acid length of less than 250 amino acids.

47. (Currently Amended) The method of claim 42, wherein the ~~NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having~~ has identity to SEQ ID NO: 1, SEQ ID NO: 14, ~~SEQ ID NO: 16, or SEQ ID NO: 18~~ that is:

- a) at least ~~80~~ 70%;
- b) at least 90%; or
- c) 100%.

48. (Currently Amended and Withdrawn) The method of claim 42, wherein the composition comprises one or more polypeptide ~~comprises~~ fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20]
- (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21]
- (c) KLGNVDFRI [SEQ ID NO: 4]
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22]
- (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23]
- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24]
- (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25]
- (h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26]
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) ~~residues Ile21–Gly182 of SEQ ID NO: 1;~~
- (ii) ~~residues Lys60–Arg181 of SEQ ID NO: 1;~~
- (iii) ~~residues Arg72–Arg181 of SEQ ID NO: 1;~~
- (iv) ~~residues Lys98–Gly182 of SEQ ID NO: 1;~~
- (v) ~~residues Lys123–Gly182 of SEQ ID NO: 1;~~
- (vi) ~~residues Ile24–Val208 of SEQ ID NO: 14;~~
- (vi) ~~residues Asp29–Val208 of SEQ ID NO: 14;~~

- ~~(vii) residues Asp29–Met215 of SEQ ID NO: 14,~~
- ~~(viii) residues Asp29–Pro209 of SEQ ID NO: 14,~~
- ~~(ix) residues Asp29–Arg245 of SEQ ID NO: 14,~~
- ~~(x) residues Asp29–Met96 of SEQ ID NO: 14, or~~
- ~~(xi) residues Trp108–Val208 of SEQ ID NO: 14.~~

49. (Currently Amended) The method of claim 42, wherein the composition comprises one or more polypeptide comprises fragment selected from at least one of SEQ ID NOs: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28]
- (b) KIMIGVERTS [SEQ ID NO: 3,10]
- (c) RIESLPIKPRG [SEQ ID NO: 5]
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29]
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30]
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31]
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]
- (h) RSSATLFFVDCNRI [SEQ ID NO: 11].

50. (Currently Amended) The method of claim 42, wherein the individual is a naive individual.

51. (Currently Amended) A method for isolating a polypeptide fragment having anti-arthritic or anti-inflammatory activity comprising:

- (i) incubating a connective tissue in a buffered autolysis medium to release a mixture of polypeptide fragments containing GAG polypeptides and non-GAG polypeptides;
- (ii) fractionating the polypeptide fragments by size to produce a fraction of ~~proteins~~ polypeptides having a molecular weight of less than 30 KDa;
- (iii) separating GAG-polypeptides from non-GAG polypeptides; and
- (iv) recovering non-GAG polypeptides having a molecular weight less than 30 KDa, and having anti-arthritic or anti-inflammatory activity.

52. (Previously Presented) The method of claim 51, wherein the autolysis medium has a pH range of:

- a) about pH 2.5 to about pH 8.5;
- b) pH 3.5 to about pH 8;
- c) pH 4 to about pH 7; or
- d) pH 4.5 to about pH 7.

53. (Currently Amended) The ~~method of claim 35, wherein said administering for preventing treats or prevents~~ an autoimmune response in ~~an~~ the individual to at least one antigenic component of cartilage, ~~comprising administering the individual the composition of claim 29.~~

54. (Previously Presented) The method of claim 53, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

55. (Previously Presented) The method of claim 53, wherein the polypeptide has an amino acid length of less than 250 amino acids.

56. (Currently Amended) The method of claim 53, wherein the ~~NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having~~ has identity to ~~SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18~~ that is:

- a) at least ~~80~~ 70%;
- b) at least 90%; or
- c) 100%.

57. (Currently Amended) The method of claim 53, wherein the composition comprises one or more polypeptide ~~comprises~~ fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20]
- (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21]
- (c) KLGNNVDFRI [SEQ ID NO: 4]
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22]
- (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23]
- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24]

- (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25]
- (h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26]
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) ~~residues Ile21–Gly182 of SEQ ID NO: 1;~~
- (ii) ~~residues Lys60–Arg181 of SEQ ID NO: 1;~~
- (iii) ~~residues Arg72–Arg181 of SEQ ID NO: 1;~~
- (iv) ~~residues Lys98–Gly182 of SEQ ID NO: 1;~~
- (v) ~~residues Lys123–Gly182 of SEQ ID NO: 1;~~
- (vi) ~~residues Ile24–Val208 of SEQ ID NO: 14;~~
- (vi) ~~residues Asp29–Val208 of SEQ ID NO: 14;~~
- (vii) ~~residues Asp29–Met215 of SEQ ID NO: 14;~~
- (viii) ~~residues Asp29–Pro209 of SEQ ID NO: 14;~~
- (ix) ~~residues Asp29–Arg245 of SEQ ID NO: 14;~~
- (x) ~~residues Asp29–Met96 of SEQ ID NO: 14; or~~
- (xi) ~~residues Trp108–Val208 of SEQ ID NO: 14.~~

58. (Currently Amended) The method of claim 53, wherein the composition comprises one or more polypeptide comprises fragment selected from at least one of SEQ ID NOs: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28]
- (b) KIMIGVERTS [SEQ ID NO: 3,10]
- (c) RIESLPIKPRG [SEQ ID NO: 5]
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29]
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30]
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31]
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]
- (h) RSSATLFDVCNRI [SEQ ID NO: 11].

59. (Currently Amended) The method of claim 42, wherein said administering induces A method of inducing cartilage formation in an the individual, comprising administering to the individual the polypeptide produced by the method of claim 29.

60. (Previously Presented) The method of claim 59, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

61. (Previously Presented) The method of claim 59, wherein the polypeptide has an amino acid length of less than 250 amino acids.

62. (Currently Amended) The method of claim 59, wherein the polypeptide NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having has identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 80 ~~70~~%;
- b) at least 90%; or
- c) 100%.

63. (Currently Amended) The method of claim 59, wherein the composition comprises one or more polypeptide comprises fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20]
- (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21]
- (c) KLGNVDFRI [SEQ ID NO: 4]
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22]
- (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23]
- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24]
- (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25]
- (h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26]
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) ~~residues Ile21–Gly182 of SEQ ID NO: 1;~~
- (ii) ~~residues Lys60–Arg181 of SEQ ID NO: 1;~~
- (iii) ~~residues Arg72–Arg181 of SEQ ID NO: 1;~~
- (iv) ~~residues Lys98–Gly182 of SEQ ID NO: 1;~~
- (v) ~~residues Lys123–Gly182 of SEQ ID NO: 1;~~
- (vi) ~~residues Ile24–Val208 of SEQ ID NO: 14;~~
- (vi) ~~residues Asp29–Val208 of SEQ ID NO: 14;~~

- ~~(vii) residues Asp29–Met215 of SEQ ID NO: 14,~~
- ~~(viii) residues Asp29–Pro209 of SEQ ID NO: 14,~~
- ~~(ix) residues Asp29–Arg245 of SEQ ID NO: 14,~~
- ~~(x) residues Asp29–Met96 of SEQ ID NO: 14, or~~
- ~~(xi) residues Trp108–Val208 of SEQ ID NO: 14.~~

64. (Currently Amended) The method of claim 59, wherein the composition comprises one or more polypeptide comprises fragment selected from at least one of SEQ ID NOs: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28]
- (b) KIMIGVERTS [SEQ ID NO: peptide 3,10]
- (c) RIESLPIKPRG [SEQ ID NO: 5]
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29]
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30]
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31]
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]
- (h) RSSATLRFVDCNRI [SEQ ID NO: 11].

65. (New) The composition of claim 29, wherein the composition comprises one or more polypeptide fragment selected from

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28]
- (b) KIMIGVERTS [SEQ ID NO: 3,10]
- (c) RIESLPIKPRG [SEQ ID NO: 5]
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29]
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30]
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31]
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]
- (h) RSSATLRFVDCNRI [SEQ ID NO: 11]

66. (New) A method of treating or preventing in an individual an immune response to an antigenic component of collagen, comprising:

administering to the individual an isolated polypeptide or fragment thereof, the polypeptide having at least 65% identity to SEQ ID NO:14; wherein said administering induces tolerance to said at least one antigenic component of collagen.